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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,951	10/06/2003	Thomas Luther	2923-571	3589
6449	7590	11/03/2005	EXAMINER	
ROTHWELL, FIGG, ERNST & MANBECK, P.C. 1425 K STREET, N.W. SUITE 800 WASHINGTON, DC 20005			HOWARD, ZACHARY C	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 11/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/679,951

Applicant(s)

LUTHER ET AL.

Examiner

Zachary C. Howard

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-61 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) _____ is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-61 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) ☐ Notice of References Cited (PTO-892) | 4) ☐ Interview Summary (PTO-413) |
| 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) ☐ Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) ☐ Other: _____ |

DETAILED ACTION

Status of Application, Amendments and/or Claims

The preliminary amendments of 10/6/03 and 5/19/04 have been entered in full. Claims 3-5, 7-9, 11, 21-24, 26-29, 31, 34, 36, 37, 41, 42-45, 47-49, 52-55, and 58-61 are amended.

Claims 1-61 are pending.

Notes

For purposes of restriction, claim 15 has been interpreted as drawn to a method of using a protein (specifically, a uPAR deletion variant) to produce antibodies.

For purpose of restriction, claims 29-31 have been interpreted as being drawn to a method of using an antibody to detect a protein (specifically, a uPAR deletion variant) in a biological sample.

For purpose of restriction, claim 38 has been interpreted as being drawn to a method of using a protein or nucleic acid for identification of an agent that will modulate the activity of a protein.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-10, 19-22, 27 and 32-35, in so far as they are drawn to a nucleic acid, vector comprising said nucleic acid, host cell comprising said vector and method for the production of a polypeptide using said host cell, pharmaceutical compositions of said nucleic acid, vector or host cell, classified (respectively) in class 536, subclass 23.1; class 435, subclass 320.1; class 435, subclass 252.3; class 435, subclass 69.1; and class 514, subclass 44, for example.

- II. Claims 11-14, 19-22 and 27, in so far as they are drawn to a protein and pharmaceutical compositions of said protein, classified (respectively) in class 530, subclass 350 and class 435, subclass 514, subclass 12.
- III. Claim 15, drawn to a method of using a protein as an immunogen to produce antibodies, classified in class 484, subclass 184.1.
- IV. Claims 16-28, 36 and 37, in so far as they are drawn to an antibody and pharmaceutical compositions of said antibody, classified (respectively) in class 530, subclass 387.9 and class 424, subclass 139.1.
- V. Claims 29-31, drawn to a method of using an antibody to detect a protein in a biological sample, classified in class 435, subclass 7.2.
- VI. Claim 38, in so far as it is drawn to a method of using a protein to identify agents that modulate the activity of the protein, classified in class 435, subclass 7.1.
- VII. Claim 38, in so far as it is drawn to a method of using a nucleic acid to identify agents that modulate the activity of the protein, classified in class, subclass class 435, subclass 6.
- VIII. Claim 39-61, drawn to a method of detecting tumors, or predicting risk of cancer, by determining the presence of a splice variant of a nucleic acid in a biological sample from a tumor, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

Inventions I, II, and IV are independent and distinct, each from each other, because they are products which possess characteristic differences in structure and function and each has an independent utility that is distinct for each invention which cannot be exchanged.

The polynucleotide of Group I and the polypeptide of Group II are patentably distinct for the following reasons: polypeptides (composed of amino acids) and polynucleotides (composed of purines and pyrimidines) are structurally distinct molecules; any relationship between them depends upon the information provided by

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the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. Furthermore, the search of the inventions of Group I and II together would impose a serious search burden. The two inventions have a separate status in the art as shown by their different classifications. In cases such as this where descriptive sequence information is provided, the protein and nucleic acid sequences are searched in databases that are not coextensive. In addition, the technical literature search is not coextensive. A protein may be described in the literature prior to the concomitant isolation and expression of the nucleic acid sequence. Similarly, there may be "classical" genetics papers that describe the gene but not the polypeptide. Furthermore, a search of the nucleic acid sequences of Group I would require an oligonucleotide search, which is not likely to result in relevant art with respect to the polypeptide of Group II.

The polypeptide of Group II and the antibody of Group IV are patentably distinct for the following reasons: while both inventions are polypeptides, Group II is a single chain molecule, whereas Group IV encompasses antibodies that comprise 2 heavy and 2 light chains containing constant and variable regions, including framework regions that scaffold the 6 complementarity determining regions involved in epitope binding. Thus, the polypeptide of Group II and the antibody of Group IV are structurally distinct molecules; any relationship between the two depends on the correlation between the scope of the polypeptides that the antibody binds and the scope of the antibodies generated upon immunization with the polypeptide.

Furthermore, searching the inventions of Group II and IV together would impose a serious burden. A polypeptide and an antibody to which the polypeptide binds have a separate status in the art as shown by their different classifications, and require different searches. A determination of novelty and unobviousness of a protein sequence requires a full-length amino acid search. However, such a search is not required to identify the antibodies of Group IV. Furthermore, antibodies that bind an epitope of a polypeptide of Group II may be known even if the polypeptide is novel. In addition, the technical literature search for the polypeptide of Group II and the antibody of Group IV is not

coextensive, e.g. an antibody may be described in the literature prior to discovery or sequencing of its binding target.

The polynucleotide of Group I and the antibody of Group IV are patentably distinct for the following reasons: polynucleotides (composed of nucleic acids), and antibodies (polypeptides composed of amino acids) are structurally distinct molecules. Any relationship between a polynucleotide and a polypeptide depends on the nucleic acid sequence open reading frame as it corresponds to the primary amino acid sequence of the encoded polypeptide. In the present claims, a polynucleotide of Group I will not encode an antibody of Group IV, and an antibody of Group IV cannot be encoded by a polynucleotide of Group I. Therefore, the polynucleotide and antibody are patentably distinct. The two inventions have a separate status in the art as shown by their different classifications. Furthermore, there would be a serious search burden because a search of the polynucleotide of Group I would not be used to determine the patentability of an antibody of Group IV and vice-versa.

Invention I is unrelated to each of Inventions III, V and VI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the nucleic acids of Invention I are not used in the method of using the protein to produce antibodies, the method of using an antibody to detect a protein in a biological sample, or a method of using a protein to identify modulators of the activity of the protein.

Invention I is related to each of groups VII and VIII as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the nucleic acid of Invention I can be used in gene therapy, which is a materially different processes of using the product.

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Invention II is related to each of groups III, V and VI as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the protein of Invention II can be used in in vitro cell culture assays or in therapeutic methods, which are materially different processes of using the product.

Invention II is unrelated to each of Inventions VII and VIII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the protein of Invention II are not used in the method of using the nucleic acid to identify modulators or in the method of using a nucleic acid to detect a splice variant in a sample.

Inventions III and IV are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the antibody can be made in a method of using the protein as an immunogen to produce antibodies, but the antibody can also made by in vitro synthetic antibody selection.

Invention IV is related to group V as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the antibody of Invention IV can be used in a method of detecting a protein in a biological sample, but it can also be used in a method of purification of a protein, which is a materially different processes of using the product.

Invention IV is unrelated to each of Inventions VI, VII and VIII. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and

they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the antibody of Invention IV is not used in the method of using a protein to identify modulators, in the method of using the nucleic acid to identify modulators or in the method of using a nucleic acid to detect a splice variant in a sample.

Although there are no provisions under the section for "Relationship of Inventions" in M.P.E.P. § 806.05 for Inventions that are directed to different methods, restriction is deemed to be proper because these methods appear to constitute patentably distinct inventions for the following reasons: Inventions III, V, VI, VII and VIII are directed to methods that are distinct both physically and functionally, and are not required one for the other. Invention III requires search and consideration of using a protein as an immunogen to produce antibodies, which is not required by any of the other Inventions. Invention V requires search and consideration of using an antibody to detect a protein in a biological sample, which is not required by any of the other Inventions. Invention III requires search and consideration of using a protein to screen for modulators, which is not required by any of the other Inventions. Invention III requires search and consideration of using a nucleic acid to screen for modulators, which is not required by any of the other Inventions. Invention III requires search and consideration of using a nucleic acid to detect a splice variant in a biological sample, which is not required by any of the other Inventions. Furthermore, the distinct steps and ingredients require separate and distinct searches.

The inventions of Groups I-VIII have a separate status in the art as shown by their different classifications and separate, non-coextensive search requirements. As such it would be burdensome to search the inventions of Groups I-VIII together.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, separate search requirements and/or divergent subject matter, restriction for examination purposes as indicated is proper.

Rejoinder under Ochiai/Brouwer

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312. In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. § 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai*, *In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is advised that for the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

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Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Bridget E. Bunner

**BRIDGET BUNNER
PATENT EXAMINER**